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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Sarvetnick *et al.*

Continuation of
USSN 09/212,531

FOR: AN ANIMAL MODEL FOR IDENTIFYING A COMMON STEM/PROGENITOR TO LIVER CELLS AND PANCREATIC CELLS

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination of the above-identified application, please amend the application as set forth below and consider the following remarks.

IN THE SPECIFICATION

At page 1, line 7, please add the following:

-- **GRANT SUPPORT**

This invention was made with United States Government support under Contract No. HD29764 by the National Institutes of Health. The United States Government has certain rights in the invention. --

IN THE CLAIMS

Please replace the pending claims with the following:

1. A transgenic non-human mammal, whose cells contain a polynucleotide, comprising: a pancreas-specific promoter operably linked to a KGF-coding polynucleotide.

2. The transgenic mammal of claim 1 wherein the pancreas-specific promoter is an insulin promoter.

3. (Amended) The mammal of claim 1, whose cells further contain a polynucleotide, comprising:
a second pancreas-specific promoter operably linked to an EGF-coding polynucleotide.

4. (Amended) The mammal of claim 1, whose cells further contain a polynucleotide, comprising:
an insulin promoter operably linked to an EGF-coding polynucleotide promoter.

5. A method for the *in vivo* proliferation of pancreatic duct cells in a mammal, comprising:
providing a pancreatic source of KGF to the mammal.

6. A method for *in vivo* production of pancreatic hepatocytes in a mammal, comprising:
providing a pancreatic source of KGF to the mammal.

7. (Amended) The method of claim 5, wherein the pancreatic source of KGF is provided by expression of a recombinant DNA molecule comprising a pancreatic specific promoter operably linked to a KGF-coding polynucleotide.

8. A method for producing pancreatic duct cells, comprising
contacting a common stem/progenitor cell to liver cells and pancreatic cells with a developmentally effective amount of KGF, wherein KGF induces common stem/progenitor cells to develop to duct cells.

9. A method for producing amylase-positive exocrine cells, comprising
contacting a common stem/progenitor to liver cells and pancreatic cells with a developmentally effective amount of KGF, wherein KGF induces common stem/progenitor cells to develop to exocrine cells.

10. A method for the *in vivo* proliferation of a common stem/progenitor to liver cells and pancreatic cells, comprising

providing a pancreatic source of KGF a proliferation-inducing growth factor to a mammal, wherein the growth factor is the expression product of a polynucleotide having a pancreatic-specific promoter operably linked with a coding polynucleotide for the growth factor.

11. The method of claim 10, wherein the pancreatic-specific promoter is an insulin promoter.

12. A method for inhibiting beta cell development in the pancreas of a mammal, comprising: injecting the subject with an inhibition-effective amount of a neutralizing α-KGF antibody.

13. A method for identifying proliferating pancreatic duct cells using PDX-1 as a marker, comprising:
    (a) contacting a pancreatic duct containing proliferating pancreatic duct cells with a reagent that binds to PDX-1; and
    (b) detecting the contact, wherein the detection identifies the duct as containing proliferating pancreatic duct cells.

14. The method of claim 13, wherein the reagent is an anti-PDX-1 antibody.

15. The method of claim 13, wherein the detection is of contact between the reagent and PDX-1 in a proliferating pancreatic duct cell.

16. The method of claim 13, wherein the proliferating pancreatic duct cell is a pancreatic stem/progenitor cell.

17. The method of claim 16, wherein the detection is of contact between the reagent and PDX-1 in a pancreatic stem/progenitor cell.

18. (New) A transgenic mouse having incorporated into its genome a polynucleotide sequence comprising a pancreas-specific promoter operably linked to a KGF-coding

polynucleotide sequence, wherein said KGF-coding polynucleotide sequence is expressed in the pancreatic cells such that said mouse exhibits in its pancreas at least one of the following morphological changes selected from the group consisting of hyperproliferation of duct cells and disorganized growth of islet of Langerhans.

19. (New) A transgenic mouse having incorporated into its genome a polynucleotide sequence comprising a pancreas-specific promoter operably linked to an EGF-coding polynucleotide sequence, wherein said EGF-coding polynucleotide sequence is expressed in the pancreatic cells such that said mouse exhibits in its pancreas at least one of the following morphological changes selected from the group consisting of hyperproliferation of duct cells, disorganized growth of islet of Langerhans, and an increase number of intra-islet ductules.

20. (New) The transgenic mouse of claim 18 further comprising incorporated into its genome a polynucleotide comprising a pancreas-specific promoter operably linked to an EGF-coding polynucleotide, wherein said EGF-coding polynucleotide and said KGF-coding polynucleotide is expressed in the pancreatic cells such that said mouse exhibits in its pancreas at least one of the following morphological changes selected from the group consisting of hyperproliferation of duct cells, disorganized growth of islet Langerhans, and increased number of intra-islet ductules, and extensive intra-islet fibrosis.

21. (New) The method of claim 6, wherein the pancreatic source of KGF is provided by expression of a recombinant DNA molecule comprising a pancreatic specific promoter operably linked to a KGF-coding polynucleotide.

REMARKS

Upon entry of the present amendments, claims 1-21 are pending. The present amendment does not introduce new matter.

Version With Markings to Show Changes

3. (Amended) The mammal of claim 1 [or 2], whose cells further contain a polynucleotide, comprising:
a second pancreas-specific promoter operably linked to an EGF-coding polynucleotide.

4. (Amended) The mammal of claim 1 [or 2], whose cells further contain a polynucleotide, comprising:
an insulin promoter operably linked to an EGF-coding polynucleotide promoter.

7. (Amended) The method[s] of claim 5 [or 6], wherein the pancreatic source of KGF is provided by expression of a recombinant DNA molecule comprising a pancreatic specific promoter operably linked to a KGF-coding polynucleotide.

18. (New) A transgenic mouse having incorporated into its genome a polynucleotide sequence comprising a pancreas-specific promoter operably linked to a KGF-coding polynucleotide sequence, wherein said KGF-coding polynucleotide sequence is expressed in the pancreatic cells such that said mouse exhibits in its pancreas at least one of the following morphological changes selected from the group consisting of hyperproliferation of duct cells and disorganized growth of islet of Langerhans.

19. (New) A transgenic mouse having incorporated into its genome a polynucleotide sequence comprising a pancreas-specific promoter operably linked to an EGF-coding polynucleotide sequence, wherein said EGF-coding polynucleotide sequence is expressed in the pancreatic cells such that said mouse exhibits in its pancreas at least one of the following morphological changes selected from the group consisting of hyperproliferation of duct cells, disorganized growth of islet of Langerhans, and an increase number of intra-islet ductules.

20. (New) The transgenic mouse of claim 18 further comprising incorporated into its genome a polynucleotide comprising a pancreas-specific promoter operably linked to an

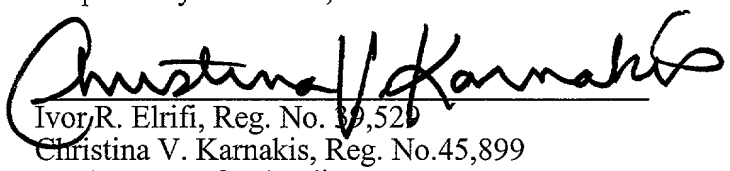
EGF-coding polynucleotide, wherein said EGF-coding polynucleotide and said KGF-coding polynucleotide is expressed in the pancreatic cells such that said mouse exhibits in its pancreas at least one of the following morphological changes selected from the group consisting of hyperproliferation of duct cells, disorganized growth of islet Langerhans, and increased number of intra-islet ductules, and extensive intra-islet fibrosis.

21. (New) The method of claim 6, wherein the pancreatic source of KGF is provided by expression of a recombinant DNA molecule comprising a pancreatic specific promoter operably linked to a KGF-coding polynucleotide.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact either of the undersigned at the telephone number provided below.

Respectfully submitted,



Ivor R. Elrifi, Reg. No. 39,529
Christina V. Karnakis, Reg. No.45,899
Attorneys for Applicants
c/o MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY AND POPEO, P.C.
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241

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